

Lyme Borreliosis

**Most Common Vector Borne
Disease in The North Hemisphere**

Diagnosis of Lyme Borreliosis

EM is the only characteristic clinical manifestation.

All other manifestations can be found in other diseases.

Diagnosis of Lyme Borreliosis

Lyme Borreliosis is in the Differential Diagnosis of Many Diseases.

More than 3 million Lyme disease tests are performed annually in the U.S.

Diagnosis of Lyme Borreliosis

**The most commonly used assays use
Whole *B. burgdorferi* as their antigen
source.**

All such assays lack specificity

Diagnosis of Lyme Borreliosis

The 41kd Flagelin cross reacts with other bacterial flagelin antigens.

- One third or more healthy adults have detectable anti-41kd antibodies.

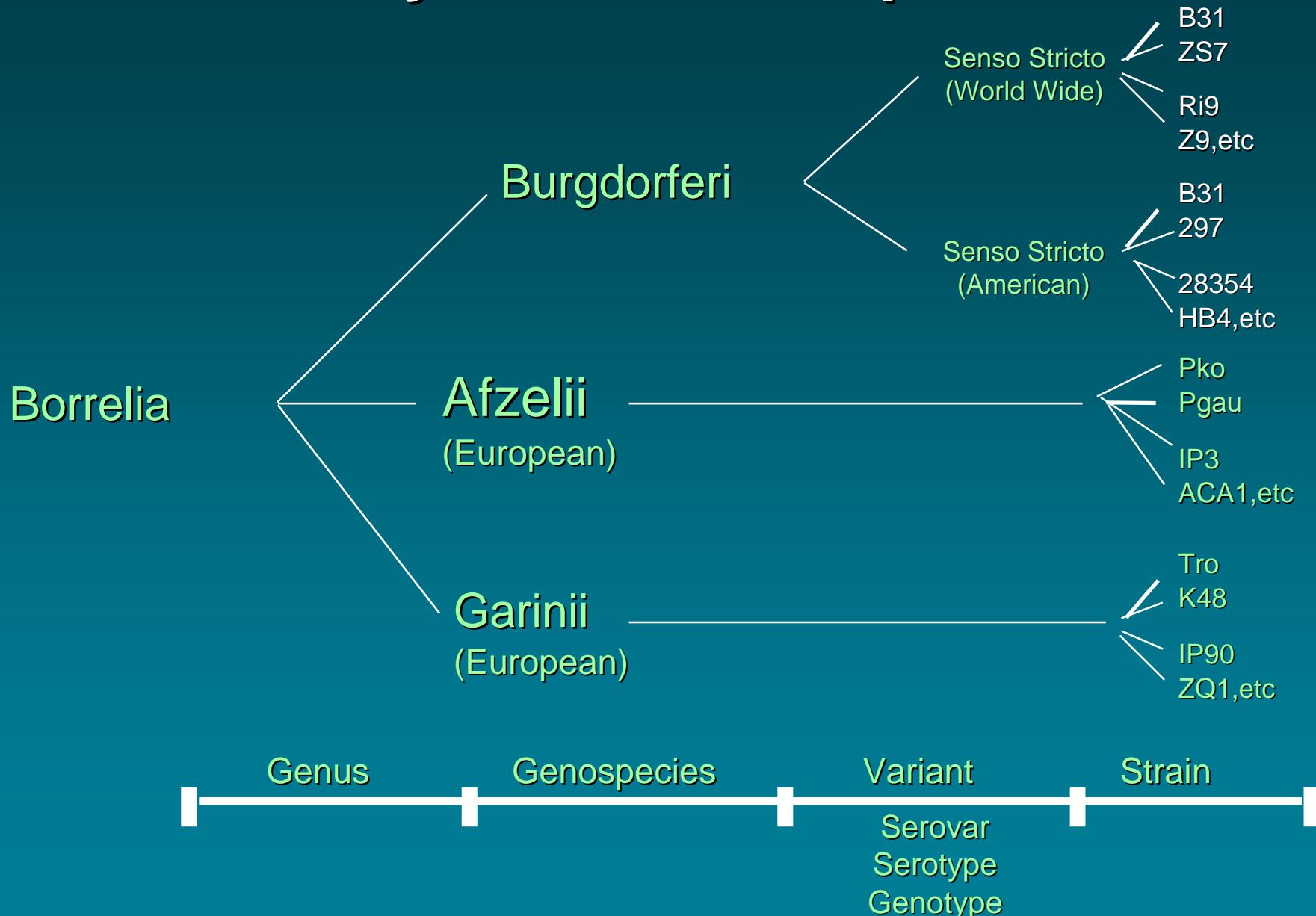
B. Burgdorferi expresses common bacterial antigens.

Borrelia burgdorferi

3 separate pathogenic
"species"

- *B. burgdorferi, senso stricto*
- *B. garinii*
- *B. afzelli*

Taxonomy of *Borrelia* Species



Rapid vs Whole Bb ELISA

	<u>ELISA</u>	<u>Rapid</u>
Early Lyme	15/30	16/30
Early Disseminated	40/60	41/60
Late Disease	30/30	30/30

Rapid vs Whole Bb ELISA

	<u>ELISA</u>	<u>Rapid</u>
Syphillis	7/20	0/20
Rheumatologic Disease	0/20	0/20
HGE	2/10	1/20
Healthy Controls	5/100	3/100

Diagnosis of Lyme Borreliosis

C6 Assay

- C6 ELISA greater specificity and sensitivity than whole *B. burgdorferi* based tests.
- Single best assay currently available.
- Greater specificity reduces cost by decreasing need for additional tests.

VIsE IR6 Peptides

IP90 CMKKDDQIAAA**MVLRGMAKDGFALK**

B31 CMKKDDQIAAA**IALRGMAKDGFALK**

VlsE IR6 Peptide ELISA

Early Erythema Migrans Serum

IP90 CMKKDDQIAAA**MVLRGMAKDGFALK** 9/33 (27%)

B31 CMKKDDQIAAA**IALRGMAKDGFALK** 11/33 (33%)

Minimal Immunodominant Region in VlsE IR6 in *B. burgdorferi* B31

Early Erythema Migrans

B31-IR6-26	CMKKDDQIAAAIALRGMAKDGKFAVK	33%
B31-IR6-18	MKKDDQIAAAIALRGMAK	36%
B31-IR6-17	MKKDDQIAAAIALRGMA	39%
B31-IR6-16Ct	MKKDDQIAAAIALRGM	24%
B31-IR6-16Nt	KKDDQIAAAIALRGMA	33% <u> </u>

Sensitivity IR6-17 vs C6 Assay

	Number of samples	B31-IR6-17	C6 Assay
		N. Pos (%)	N. Pos (%)
Early Lyme			
Localized EM, at presentation (acute)	48	21 (44%) 	13 (27%) 
Acute disseminated	7	5 (71%)	5 (71%)
Convalescent, on antibiotic	20	13 (65%)	11 (55%)
Late Lyme			
Neuroborreliosis. and arthritis	11	10 (91%)	9(82%)
Post-treatment LD Syndrome	14	7(50%)	7(50%)

Pos, > 3 STD using normal sera as cutoff

 p Value by McNemar's Exact Test for correlated proportions is <0.01 (significant);

Specificity IR6-17 vs C6 Assay

	N. of samples	B31-IR6-17 N. Pos (%)	C6 Assay N. Pos (%)
Rheumatoid Arthritis	40	1 (3%)	1 (3%)
SLE	13	0 (0%)	1 (8%)
Syphilis	19	2 (11%)	3 (16%)
H. pylori	55	2 (4%)	6 (11%)
Normals (endemic)	28	0 (0%)	1 (4%)
Specificity 	155	5 (97%)	12 (92%)

Pos, > 3 STD using normal sera as cutoff

 p Value by McNemar's Exact Test for correlated proportions is <0.01 (significant)

Additional Targets

BBK32*

Linear OspC Epitopes

FlaB Internal Fragment

Additional Targets OspC

Linear OspC Epitopes

- C10 peptide (PVVAEESPKKP) at the C-terminal end of OspC*
- Conserved region positions 9–22 consisting of 14 amino acid (ILMTLFLFISCNNS)**

*Bacon et al. J Infect Dis. 187:1187-99; 2003

**Ikushima et al. FEMS Immunol Med Microbiol. 29:15-21; 2000

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